

# Case Report Rapport de cas

## Hypertrophic osteopathy associated with hepatocellular carcinoma in a dog

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**Abstract** — A 9-year-old spayed female dog diagnosed with hepatocellular carcinoma and hypertrophic osteopathy was negative for additional lesions on computed tomography of the thorax and abdomen. Resection of the affected liver lobe resulted in resolution of clinical signs. This is the first case of hypertrophic osteopathy secondary to hepatocellular carcinoma.

**Résumé** — **Ostéopathie hypertrophique associée à un carcinome hépatocellulaire chez un chien.** Un carcinome hépatocellulaire et de l'ostéopathie hypertrophique ont été diagnostiqués chez une chienne stérilisée âgée de 9 ans mais était négative par tomodensitométrie pour des lésions additionnelles au thorax et à l'abdomen. La résection du foie touché a produit une résolution des signes cliniques. C'est le premier cas d'ostéopathie hypertrophique secondaire à un carcinome hépatocellulaire.

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**A** 9-year-old spayed female mixed breed dog, weighing 23 kg, was presented to the Oncology Department of the University of Florida for a liver mass previously identified on abdominal ultrasound by the referring veterinarian. One-month duration of decreased appetite and swelling in all 4 limbs were noted.

### Case description

On presentation the dog was bright, alert, and responsive. She was ambulatory, but very stiff upon walking. All 4 limbs were painful to touch and had distal edematous swelling, extending from mid-tibia to mid-metacarpal and tarsal regions. The rectal temperature was elevated at 39.9°C. Mucoïd ocular discharge and scleral hyperemia were noted in both eyes. The remainder of the physical examination was unremarkable.

Serum biochemistry showed elevations in alkaline phosphatase [470 U/L; reference range (RR): 8 to 114 U/L] and alanine aminotransferase (72 U/L; RR: 18 to 64 U/L). Complete blood (cell) count (CBC) showed 1+ anisocytosis and 1+ target cells present. Results from the hematology indicated a mature neutrophilia ( $13.0 \times 10^3/\mu\text{L}$ ; RR:  $2.7$  to  $8.9 \times 10^3/\mu\text{L}$ ). The results of the urinalysis were unremarkable.

Abdominal ultrasound revealed a well-defined heteroechoic 9 cm  $\times$  7 cm lobular mass within the left aspect of the liver (Figure 1). This mass had multiple, irregular anechoic regions centrally causing distal acoustic enhancement. Color Doppler showed moderate vascularity within the peripheral aspect of the mass. Additionally, multiple well-defined, hypoechoic nodules measuring up to 8 mm were identified within the left division of the liver. A small volume of anechoic fluid was seen within the peritoneal cavity. Ultrasound-guided fine-needle aspiration of the liver mass was inconclusive for neoplasia, with only mild hepatocellular atypia present. Cytology of peritoneal effusion showed a non-septic exudate with no evidence of neoplastic cells.

Three-view thoracic radiographs revealed no intrathoracic abnormalities. Radiographs of both the left and right tarsi revealed well-defined, smooth, mixed lamellar and columnar osseous proliferation along the tibia, fibula, tarsal, and metatarsal bones bilaterally (Figure 2). Several smoothly margined, oval, up to 3.6 mm mineralized structures were noted just proximal to the calcaneus tuber bilaterally. Moderate soft tissue thickening was present surrounding the tarsi and metatarsi. These radiographic findings were consistent with hypertrophic osteopathy (HO) with possible fracture fragments of the osseous proliferation.

Computed tomography (CT), with and without intravenous positive contrast, was performed of the thorax, extremities, abdomen, and pelvis. The only intrathoracic abnormality was mildly enlarged sternal lymph nodes, which measured up to 1.8  $\times$  0.8  $\times$  0.8 cm. A well-defined, lobular, heterogenous mass was seen within the left lateral liver lobe causing medial displacement of the fundic portion of the stomach. Multiple, small, mineral attenuating foci were seen centrally within the mass. Following intravenous contrast administration, multiple

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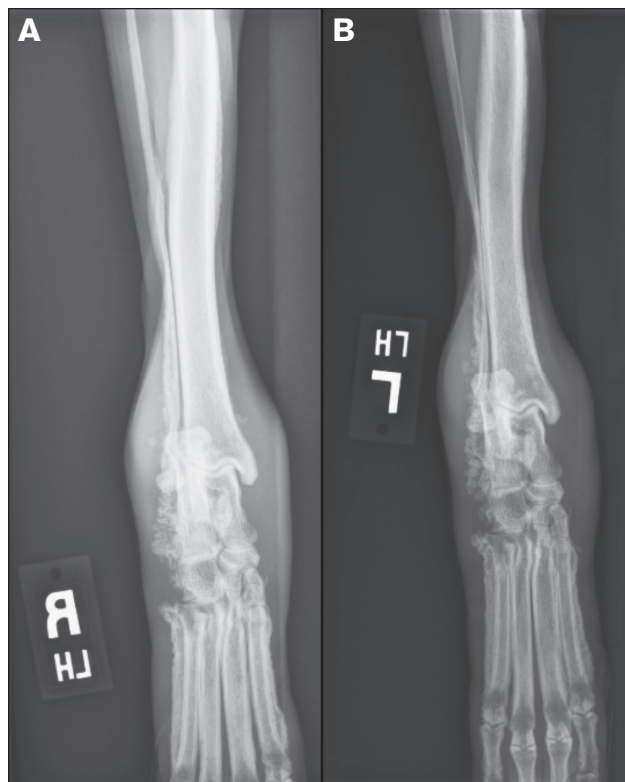
**Figure 1.** Transverse ultrasonographic view showing a well-defined 9 cm × 7 cm lobular mass within the left aspect of the liver, scant peritoneal effusion, and multifocal hepatic nodules.

marginal and central vascular structures were seen during the arterial phase. Heterogenous contrast enhancement of the mass similar to that of the surrounding hepatic parenchyma was seen during the portal venous and venous phases. Multiple, irregular, but well-defined fluid attenuating regions that did not contrast enhance were seen within the central region of the mass. Multifocal hyper-attenuating, contrast enhancing splenic nodules were also seen. Computed tomography of the thoracic limbs included within the field of view, showed smooth, continuous, mixed columnar and lamellar periosteal proliferation along the antebrachii proximal to the mid aspect of the humeri similar to what was described on the radiographic images of the pelvic limbs (Figure 3). Based on these imaging features, a diagnosis of HO was made and the patient was treated with Deracoxib (Novartis Animal Health US, Greensboro, North Carolina, USA), 2 mg/kg body weight (BW), PO, q24h for 14 d.

Exploratory laparotomy was performed, revealing a nodular mass confined to the left lateral liver lobe, 2 moderately enlarged hypogastric lymph nodes, and an area of the mesentery that appeared to be grossly thickened and irregular. A left lateral liver lobectomy was performed using a thoracoabdominal (TA) stapling device. The enlarged lymph nodes were excised and a biopsy of the irregular area of the mesentery was performed. Initial recovery was uneventful and the patient was discharged 24 h later. Contact with the owner 7 d after discharge indicated that the lameness had resolved and the dog was no longer receiving Deracoxib.

Gross examination of the excised left liver lobe revealed an expansive, poorly demarcated mass with well-demarcated nodules. Histologically, the nodules contained a dense sheet of polygonal cells forming plates and cords separated by variable amounts of fibrosis. Mild anisocytosis and anisokaryosis were present with a mitotic index of 5 per 10, 400× fields. Based on these histological findings, a diagnosis of hepatocellular carcinoma (HCC) was made. The irregular portion of mesentery submitted for histopathology showed granulation tissue present. The lymph nodes were normal with no evidence of metastasis.

Seven months after surgery, the owner stated that the dog continued to behave normally. The limbs were no longer swollen and the dog showed no evidence of lameness and was not receiving any analgesic medication. Normal appetite and activity



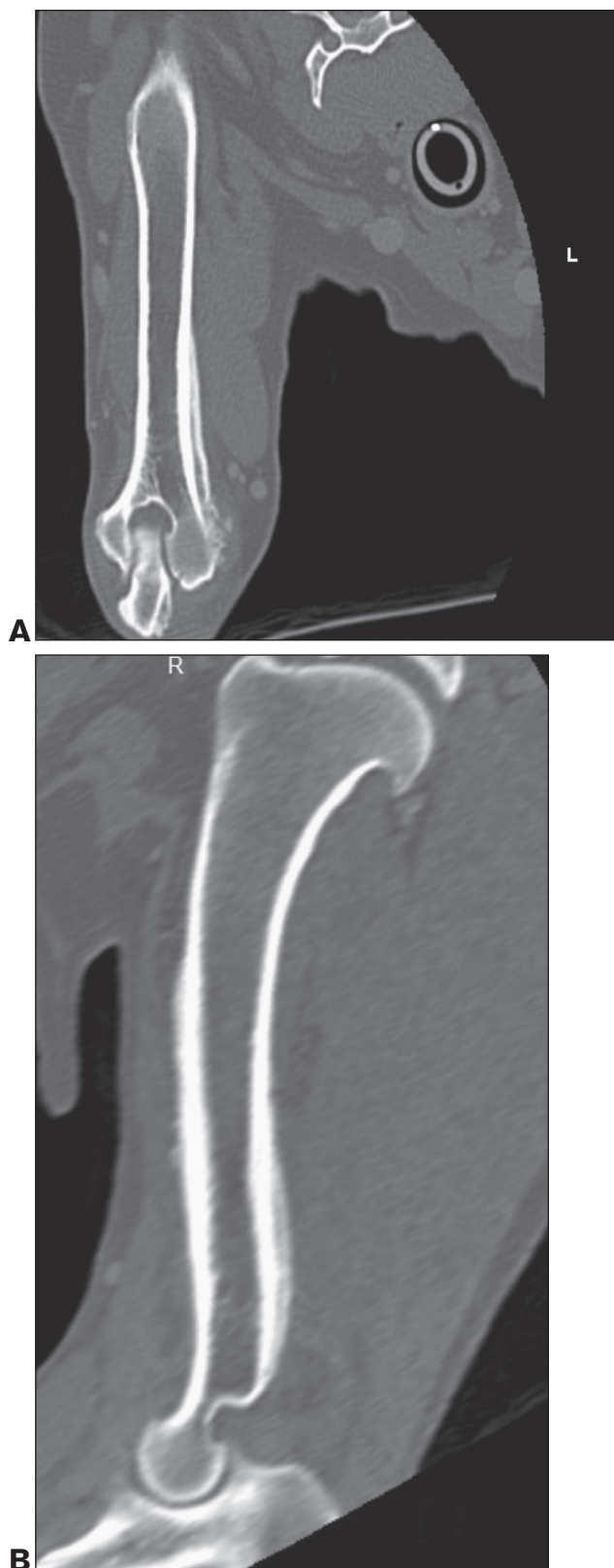
**Figure 2.** Dorsoplantar views of the right (A) and left (B) tarsi showing bilateral well-defined, smooth, mixed lamellar and columnar osseous proliferation along the tibia, fibula, tarsal, and metatarsal bones.

had resumed. Repeat radiographs of the limb and thorax, along with abdominal ultrasound were offered, but were declined by the client.

## Discussion

This report demonstrates resolution of clinical signs associated with suspected HO following surgical excision of a primary liver tumor. Hypertrophic osteopathy is a rare disease characterized by periosteal proliferation along the diaphysis of long bones, resulting in cortical thickening (1,2). It most commonly occurs bilaterally, and often in all 4 limbs, along an area of periosteum that is not associated with tendon insertions or adjacent bones (3,4). The clinical signs of HO typically include swollen limbs, lameness, lethargy, ocular signs, and pain on palpation of limbs (5). Fever is often reported, and may be due to tumor-associated or immune-mediated pyrogenic cytokines (3,5). Regression of clinical signs has been reported to occur 2 wk after surgical excision or treatment of the primary cause, with the bone lesions regressing gradually over several months (1,4).

The pathogenesis of HO is not well understood, and several theories have been proposed (1). One theory suggests it may be due to increased poorly oxygenated blood flow to the limbs producing local passive congestion (4,6). Poor tissue oxygenation stimulates proliferation of connective tissue, including the periosteum and synovial membrane (4). This depression of blood flow has been theorized to be caused by a neural vascular reflex, originating in the thorax and carried by afferent vagal fibers.



**Figure 3.** Computed tomography of the left and right thoracic limbs. A – Coronal view of left thoracic limb. B – Sagittal view of right thoracic limb. Circumferentially surrounding the left and right proximal radius, ulna and humerus, there is smooth, continuous periosteal proliferation that transitions to discontinuous and irregularly margined at the level of the right lateral humeral epicondyle and transitions to cuboidal at the level of the left medial humeral epicondyle.

This theory has been supported by studies showing regression of clinical signs after performing a vagotomy (1,4).

Hypertrophic osteopathy has been reported as developing secondary to both malignant and non-malignant diseases (7). The most commonly reported causes are primary and metastatic lung disease; however, infections such as spirocercosis, dirofilariasis, and bacterial endocarditis have been reported (1,3–5,7,8); reports of abdominal tumors in the literature are less common (1,3–5,7,8).

In this report, we describe a case in which hypertrophic osteopathy is present with no intrathoracic lesions, but instead a primary liver tumor. Hepatocellular carcinoma is the most common hepatic neoplasm in dogs (9,10). In humans, HCC is linked to hepatitis and cirrhosis, but in dogs and cats, the etiology is unclear (10,11). The prognosis for liver tumors is dependent on histology and morphology, and clinical presentation. There are 3 morphologic subtypes of HCC: diffuse, nodular, and massive (9). Massive tumors, defined as a solitary mass confined to a single liver lobe, tend to have a better prognosis due to their susceptibility for surgical resection, compared with nodular or diffuse tumors. Sixty-one percent of all canine HCC tumors have massive morphology (9–11). Right-sided liver tumors may have a poorer prognosis as the risk of intraoperative death increases due to hemorrhage and involvement of the caudal vena cava (10).

In both dogs and cats with hepatic tumors that have a massive morphologic appearance, surgical excision is the treatment of choice (10). In a study including 42 dogs, the median survival time after surgical excision of a massive liver tumor was not reached due to most of the dogs being either still alive or dead from an unrelated cause (9,10). Local tumor recurrence after a liver lobectomy of a massive HCC is 0% to 13% in dogs (10).

In summary, we described a patient which was diagnosed with HO secondary to HCC. Improvement of clinical signs occurred after surgical resection of the affected liver lobe. To our knowledge, this is the first report of HO secondary to a liver tumor in the dog.

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